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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,391	12/22/2003	Timothy Raymond Hirst	00833-P0043A	7178

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EXAMINER	
MONTANARI, DAVID A	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
11/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/743,391	HIRST, TIMOTHY RAYMOND	
	Examiner	Art Unit	
	David Montanari	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,10-12,17,18,21,26 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10-12,17,18,21,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants amendments filed 9/4/2007 have been entered.

2. Claims 1, 12, 17 and 21 have been amended.

3. Claims 4-9, 13-16, 19, 20 and 22-25 are cancelled.

4. A copy was received of UK Patent application 01153823.4.

5. The sequence listing with the appropriate annotations has been received.

6. Claims 1-3, 10-12, 17, 18, 21, 26 and 27 are examined in the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 10-12, 17-18, 21 and 26-27 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *in vitro* method of delivering a peptide to a cell expressing GM-1 ganglioside receptors on the surface of said cell comprising contacting said cell with a mutant B-subunit of *E. coli* heat labile enterotoxin (EtxB) or a mutant B-subunit of *Vibrio cholerae* cholera toxin (CtxB) covalently linked to said peptide, said mutant EtxB or mutant CtxB comprising one of the following point mutations within the region spanning amino acid residues E51 to I58 of the β 4-α2 loop of EtxB or CtxB: CtxB(E51A), CtxB(Q56A), CtxB(H57A) and EtxB(H57S), thereby delivering said peptide into said cell; and a kit comprising said mutant EtxB or mutant CtxB covalently linked to said peptide; does not reasonably provide enablement for a method of delivering

any agent to any target cell comprising contacting said cell with any mutant EtxB or any mutant CtxB, thereby delivering said agent to said cell resulting in treatment of the breadth of disorders and diseases encompassed by the claims for reasons of record in the office actions mailed 9/22/2006 and 5/1/2007.

Response to Arguments

Applicants argue in amendment filed 9/4/2007 that the physiological processes of antigen uptake and presentation operate in exactly the same way in a living cell in vivo as they do in a living cell in vitro in cell culture. Applicant continues that data obtained using in vitro cell culture is therefore entirely representative of peptide delivery which would occur in vivo using EtxB/CtxB mutants. Applicants continue that at the priority date the skilled person would be well aware of routes of administration, dosage and formulations that may be achieved to be effective in immunization with CtxB, EtxB or their fusion proteins. Applicants cite and provide several references by Svennerholm et al., Bergquist et al., Kozlowski et al., Jerborn et al., and Scharton-Kerston et al., to demonstrate different routes that the claimed invention may be administered. Applicant continues that the present claims do not relate to methods of treatment rather they relate to methods of delivering a peptide into the MHC class I antigen processing pathway of an antigen presenting cell and that the working examples demonstrate this to be an effective method for this purpose. These arguments are not persuasive.

Applicant has argued that the claimed method is not a method of treatment. However lines 11-13 on page 1 of the specification state "In particular, the present invention relates to the

use of mutant forms of EtxB or CtxB as vehicles to deliver an agent to a target site for the treatment of a disease or condition in a subject in need of the same". A continued reading throughout the specification further details and states that the claimed invention is amounting to a method of treatment. While the claims may not use the word "treatment", the specification is very clear that this treatment of a disease is a preferred embodiment with the claimed invention and thus the examination and rejection under 35 USC 112, first paragraph, enablement is proper. Starting on page 6 and continuing through page 9 of the Final rejection mailed on 9/22/2006 these issues of treatment were addressed in detail. Particularly, Plant et al., in summarizing the teachings of Bergerot and Sun discussed the requirements and challenges for using the claimed method. Further Michl et al. discussed the challenges of bacterial toxins as therapeutic agents for cancer. While Applicant has argued that the pending claims are not a method of treatment, the specification teaches otherwise, and which specific issues regarding using the claimed method still exist and have not been addressed. While it is appreciated that possible routes of administration are detailed in the art with relation to the claimed invention, these teachings do not overcome the rejection of record. The references provided by Applicant summarize different routes of administration such as intranasal (Bergquist et al.), vaginal (Kozlowski et al.), rectal (Jertborn et al.) and transcutaneous (Scharton-Kerston et al.) for using cholera toxin in vaccination. However none of these references address the specific issues that have been set forth regarding the enablement of the claimed method as a method of treatment. While they do address specific issues brought up in the previous office action regarding routes of administration, none of these references individually or combined teach the skilled artisan how to

overcome the challenges of using the claimed method for treatment. Thus the rejection is maintained for the reasons above and of record.

No claims are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari whose telephone number is 1-571-272-3108. The examiner can normally be reached on M-Tr 8-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 1-571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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